34. Coffee drinking

Details of the six studies found which gave information on the risk of lung cancer in relation to coffee drinking are shown in Table 34. Five relative risks, ranging from 0.8-7.0, were given, of which four were above 1.00. One study reported that bronchial cancer cases drank more coffee than controls but did not give detailed results. Finally, one study compared non-coffee drinkers to coffee drinkers, rather than vice versa, and estimated relative risks of 2.07 for men and 1.38 for women who did not drink coffee.

With the exception of the study by Dean, no account appeared to have been taken of consumption of other hot beverages, such as tea. Thus, it is possible that in these studies non-drinkers of coffee could in fact have been consumers of other hot drinks, which may have led to inaccuracies.

Not surprisingly then, IARC described the evidence for the carcinogenicity of coffee drinking to humans as "inadequate" [3].

Table 34: Estimates of relative risk for coffee drinking

Study	Population	Relative risk (95% limits)
Denoix et al (1958)	French men	Bronchial cancer cases drank more coffee than controls
Heuch et al (1983)[1]/ Jacobsen et al (1986)[1]	Norwegian residents	1.8
Schuman (1985)[2]	US men	7.0
Nomura et al (1986)[1]	Japanese men	1.4
Dean et al (1987)	UK male non-coffee drinkers	2.07
	Female non-coffee drinkers	1.38
Mettlin (1989)[1]	US residents, caffeinated coffee	1.3(0.9-1.8)
	Decaffeinated coffee	0.8(0.5-1.3)

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Source: https://www.industrydocuments.ucsf.edu/docs/kmbl0000

Footnote to Table 34

1 From International Agency for Research on Cancer (1991)

2 From Rowland (1985)

References

1. Dean G, Lee PN, Todd GF and Wicken AJ (1977) Tobacco Research Council research paper 14.

2. Denoix PF, Schwartz D and Anguera G (1958) French investigation into the etiology of broncho-pulmonary cancer. Detailed analysis. Bull Assoc Franc pour l'etude du Cancer, 49: 1-37.

3. International Agency for Research on Cancer (1991) Monographs on the evaluation of carcinogenic risks to humans. Volume 51: Coffee, tea, mate, methylxanthines and methylgloyoxal, 41-197. IARC, Lyon.

4. Rowland WD (1985) Personal communication

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Source: https://www.industrydocuments.ucsf.edu/docs/kmbl0000

35. Coke production

Several studies have concerned themselves with the potential risks between coke production and lung cancer, and details of them are given in Table 35. Eleven standardized mortality ratios (SMR) were calculated, and these ranged from 117 to 367. Nine studies gave estimates of relative risk from 1.00-44.00, with all but one being above 1.00. One proportional mortality ratio of 149 was also given, while the remaining study simply stated that 12 lung cancers were observed in gas-generator workers compared to none in workers in other areas.

When making an assessment of the possible risk of working in the coke production industry, several potential problems in the design of some of the studies should be borne in mind. Workers in coke production plants may be exposed to many substances to a varying degree, including aldehydes, amines, ammonia, arsenic compounds, asbestos, carbon compounds, hydrocarbons, hydrogen compounds, mercaptans, nitrogen heterocyclics, oxygen heterocyclics, phenols, polynuclear aromatic hydrocarbons, silica, sulphur compounds and thiocyanates. As only one study (Mazumdar) took objective measurements, of benzene concentrations, in the workplace, the exact nature of the subjects' exposures is impossible to ascertain.

The design of the study by Reid and Buck, in which the SMRs are based on a working population with only a short period of follow-up during which death might have occurred, may have led to a serious underestimation of the risk involved. Conversely, the use of a "precision factor" to weight the relative risks from various different plants in the study by Redmond et al (1972) increased the SMR over that calculated directly. Problems were also noted in the study by Radford, due to under-identification of deaths, loss of terminated workers, and lack of age corrections, and a difficulty in assessing how the reported excesses relate to coke-oven workers. Other potential sources of inaccuracy noted in some of the studies included small numbers of subjects, possible selection factors, imprecise work histories obtained from next-of-kin respondents, and differences in the source of information on occupation for cases and controls [1].

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Source: https://www.industrydocuments.ucsf.edu/docs/kmbl0000

Despite these drawbacks, IARC stated that there was "sufficient" evidence for the carcinogenicity of certain exposures in the coke production industry to humans, and suggested that a possible causative agent may be coal-tar fumes [1,2].

Table 35: Estimates of relative risk/standardized mortality ratio for workers in coke production

Study	Population	Relative risk (95% limits)
Kennaway and Kennaway (1936, 1947)[1]	E/W gas stokers/coke-oven chargers	284*
Kuroda (1937)[1]	Japanese gas-generator workers	12 lung cancers compared to none in workers in other areas
Reid and Buck (1956)[1]	English coking plant workers	140*
Kawai et al (1967)[1]	Japanese gas-generator workers	44.0
Lloyd and Ciocco (1969)[1]	US non-white coke plant workers	342*[2]
Lloyd (1971)[1]	US coke-oven workers	248*[2]
Redmond et al (1972)[1]	US/Canadian coke-oven workers	2.85($p<0.05$)
Mazumdar et al (1975)[1]	US/Canadian coke-oven workers	13.65
Sakabe et al (1975)[1]	Japanese coke-oven workers	128*
Radford (1976)[1]	US steel company workers	149[3]
Davies (1977)[1]	Welsh coke-oven workers	1.00
OPCS (1978)	E/W coal gas/coke oven furnacemen	180*[4]
Axelson et al (1979)[1]	Swedish coke-oven workers	>1.00($p<0.05$)
Lloyd (1980)[1]	US coke-oven workers	6.94($p<0.05$)
Redmond et al (1981)[1]	US coke-oven workers	2.63($p<0.05$)
Logan (1982)	UK men making coal/gas/coke - 1931	367*
	1951	129*
	1961	152*
	1971	178*

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Source: https://www.industrydocuments.ucsf.edu/docs/kmbl0000

Table 35 continued

Blot et al (1983)[1]	US coke-oven workers	1.2
Hurley et al (1983)[1]	British coke-oven workers	117*
Redmond (1983)[5]/Rockette and Redmond (1985)[5]	US coke-oven workers	>1.00(p<0.05)

E/W = English/Welsh

* Standardized mortality ratio

1 From International Agency for Research on Cancer (1984)

2 Cancers of respiratory tract

3 Proportional mortality ratio

4 Estimated from data given

5 From International Agency for Research on Cancer (1987)

References

1. International Agency for Research on Cancer (1984) Monographs on the evaluation of the carcinogenic risk of chemicals to humans. Volume 34: Polynuclear aromatic compounds, part 3, industrial exposures in aluminium production, coal gasification, coke production, and iron and steel founding, 101-132. IARC, Lyon.

2. International Agency for Research on Cancer (1984) Monographs on the evaluation of carcinogenic risks to humans. Supplement 7: Overall evaluations of carcinogenicity: An updating of IARC monographs volumes 1 to 42, 176-177. IARC, Lyon.

3. Logan WPD (1982) Cancer mortality by occupation and social class 1851-1971. HMSO, London.

4. Office of Population Censuses and Surveys (1978) Occupational mortality: The Registrar General's decennial supplement for England and Wales, 1970-72. HMSO, London.

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36. Cooking over coal-fired stove

Only two studies could be found which gave data relevant to an investigation of the possible association between lung cancer risk and the use of a coal-fired stove for cooking, and details of these are given in Table 36. One study estimated a relative risk of 1.88, and while the other reported a positive association, no detailed results were presented.

Therefore, while the evidence shown in the table appears to suggest a positive relationship between lung cancer and cooking over a coal-fired stove, with so little available data it is not really clear whether such an association does exist.

Table 36: Estimates of relative risk for cooking over a coal-fired stove

Study	Population	Relative risk (95% limits)
Chen et al (1990)	Chinese residents	Positive association
Liu et al (1993)	Chinese residents	1.88(1.12-3.15)

References

1. Chen BH, Hong CJ, Pandey MR and Smith KR (1990) Indoor air pollution in developing countries. Wld Hlth Statist Quart, 43, 127-138.

2. Liu J-Z, Hu H-S, Hu Y-H, Lu P and Hao L-Y (1993) A study on the relation between indoor exhaust and lung cancer. Proc Indoor Air, 1, 489-492.

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Source: https://www.industrydocuments.ucsf.edu/docs/kmbl0000

37. Cooking with wok

Table 37 gives details of the only study found which attempted to relate lung cancer risk to cooking with a wok. Six relative risks were estimated for various indices of wok cooking, and these ranged from 1.4-2.8.

Although the findings of this study are suggestive of an association between lung cancer risk and cooking with a wok, results from more studies are needed before the relationship can be confirmed.

Table 37: Estimates of relative risk for cooking with a wok

Study	Population	Relative risk (95% limits)
Gao et al (1987)	Chinese women reporting frequent eye irritation	1.4(0.9-2.3)[1]
		2.8(1.8-4.3)[2]
	Some/frequent eye irritation and some/considerable household smokiness	2.6(1.8-3.7)
	Stir frying 30+ dishes per week	2.6(1.3-5.0)
	Deep frying 3+ dishes per week	1.9(0.5-6.8)
	Boiling 12+ dishes per week	2.2(1.3-3.7)

1 Users of soybean oil

2 Users of rapeseed oil

References

1. Gao Y-T, Blot WJ, Zheng W et al (1987) Lung cancer among Chinese women. Int J Cancer, 40, 604-609.

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Source: https://www.industrydocuments.ucsf.edu/docs/kmbl0000

38. Cooking with wood/straw

Table 38 gives details of the only study found which attempted to relate lung cancer risk to the use of wood or straw as a fuel for cooking. A relative risk of 1.77 was estimated.

With only one study reporting it is not really possible to evaluate the potential carcinogenicity of wood or straw used as a cooking fuel.

Table 38: Estimate of relative risk for cooking with wood/straw

Study	Population	Relative risk (95% limits)
Sobue (1990)	Japanese women	1.77(1.08-2.91)

References

1. Sobue T (1990) Association of indoor air pollution and lifestyle with lung cancer in Osaka, Japan. Int J Epidemiol, 19, S62-S66.

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Source: https://www.industrydocuments.ucsf.edu/docs/kmbl0000

39. Cooks

Only four studies were found which gave data relevant to an investigation of the possible association between employment as a cook and the risk of lung cancer, and these are detailed in Table 39. Two relative risks, of 0.7 and 1.82, were estimated, along with two proportional mortality ratios, of 100 and 103, and two proportional registration ratios, of 124 and 130. One study observed a mortality rate of 3.2 per 1000 per year.

It has been suggested that the excess of lung cancers seen in cooks may be caused by the fumes generated during cooking, particularly frying [2,3], and also that frequent tasting of hot food may cause thermal irritation of the upper aerogastric tract [3]. However, the evidence for a possible association between lung cancer risk and employment as a cook presented here is hardly conclusive, and even if a risk does exist, it does not appear to be very large.

Table 39: Estimates of relative risk/mortality ratio for employment as a cook

Study	Population	Relative risk (95% limits)
Boucot et al (1972)	US male bakers/pastry cooks/ chefs/cooks	3.2[1]
OPCS (1978)	E/W male cooks - aged 15-64	100[2]
	Aged 65-74	103[2]
	Registrations, 1966-7	130($p<0.01$)[3]
	1968-9	124($p<0.05$)[3]
Coggon and Wield (1993)	UK army cooks	1.82(1.25-2.57)
Kjaerheim and Andersen (1993)	Norwegian male cooks	0.7(0.2-1.7)[4]

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Source: https://www.industrydocuments.ucsf.edu/docs/kmbl0000

Table 39 continued

E/W = English/Welsh

1 Per 1000 per year

2 Proportional mortality ratio

3 Proportional registration ratio

4 Standardized incidence ratio

References

1. Boucot KR, Weiss W, Seidman H, Carnahan W and Cooper DA (1972) The Philadelphia pulmonary neoplasm research project: basic risk factors of lung cancer in older men. Am J Epidemiol, 95, 4-16.

2. Coggon D and Wield G (1993) Mortality of army cooks. Scand J Work Environ Health, 19, 85-88.

3. Kjaerheim K and Andersen A (1993) Incidence of cancer among male waiters and cooks: Two Norwegian cohorts. Cancer Causes and Control, 4, 419-426.

4. Office of Population Censuses and Surveys (1978) Occupational mortality: The Registrar General's decennial supplement for England and Wales, 1970-72. HMSO, London.

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Source: https://www.industrydocuments.ucsf.edu/docs/kmbl0000

40. Cushing's syndrome

Table 40 gives details of the three studies which attempted to relate the risk of lung cancer to Cushing's syndrome, a disorder due to the excessive secretion of corticosteroid hormones by the adrenal cortex. A total of 24 cases of lung cancer were associated with the syndrome.

It was suggested that the association of the two conditions might arise from secretion of hormones by the tumour, or that both conditions may be due to pituitary-hypothalamic or adrenal over-activity. However, in the absence of any risk estimates it is not possible to determine the relationship between lung cancer and Cushing's syndrome, or the cause of any such association if it does exist.

Table 40: Observations for Cushing's syndrome

Study	Population	Observations
Allott and Skelton (1960)	Hospital patients	18 lung cancer cases associated with Cushing's syndrome
Vogel et al (1961)	Hospital patients	5 lung cancer cases associated with Cushing's syndrome
Marks et al (1963)	US male	1 lung cancer case associated with Cushing's syndrome

References

1. Allott EN and Skelton MO (1960) Increased adrenocortical activity associated with malignant disease. Lancet, ii, 278-283.

2. Marks LJ, Russfield AB and Rosenbaum DL (1963) Corticotropin-secreting carcinoma. JAMA, 183, 115-117.

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Source: https://www.industrydocuments.ucsf.edu/docs/kmbl0000

3. Vogel MD, Keating FR and Bahn RC (1961) Acute Cushing's syndrome associated with bronchogenic carcinoma. Proc Mayo Clinic, 36, 387-393.

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Source: https://www.industrydocuments.ucsf.edu/docs/kmbl0000

41. DDT

Table 41 gives details of the studies which investigated the possible association between lung cancer risk and exposure to DDT. Five relative risks were estimated, ranging from 0.91-1.8, of which all but one were above 1.00. Two standardized mortality ratios, of 156 and 180, were also calculated. Additionally, one study reported five cases of lung cancer associated with inhalation of DDT among a group of patients with granulomatous disease of the lungs.

Only the study by Austin took objective measurements of exposure to DDT, by measuring serum levels of the chemical. Two other studies (Blair, Ditraglia) did at least attempt to quantify exposure by recording the length of time workers were exposed to DDT. However, no information on the level of exposure was available from the other studies. Thus, inaccuracies could have been introduced into them. Furthermore, several of the studies (Bartel, Blair, Wang and MacMahon, Wong) stated that workers were exposed to other substances, usually other pesticides, in addition to DDT, making an analysis of the effects of DDT alone very difficult.

Therefore, IARC felt there was "inadequate" evidence for the carcinogenicity of DDT to humans [1], and in a later review, described it as only "possibly carcinogenic" [2].

Table 41: Estimates of relative risk/standardized mortality ratio for exposure to DDT

Study	Population	Relative risk (95% limits)
Pimentel and Menezes (1979)[1]	Patients with granulomatous disease of the lungs	Five lung cancer cases reported
Wang and MacMahon (1979)[1]	Pesticide applicators	>1.00
Bartel (1981)[1]	Agricultural workers	180(140-240)*
Ditraglia et al (1981)[2]	US DDT manufacturing workers	1.3(0.34-3.2)
Blair et al (1983)[1]	Pesticide applicators	>1.00
Wong et al (1984)[1]	Male DDT manufacturing workers	156(74-286)*[3]
Wicklund et al (1988)[2]	US orchard workers	0.91(0.4-2.1)[3]
Austin et al (1989)[2]	US adults	1.8(0.5-6.2)[3]

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Source: https://www.industrydocuments.ucsf.edu/docs/kmbl0000

Footnote to Table 41

* Standardized mortality ratio

1 From International Agency for Reseach on Cancer (1987)

2 From International Agency for Reseach on Cancer (1991)

3 Tumours of respiratory system

References

1. International Agency for Research on Cancer (1987) Monographs on the evaluation of carcinogenic risks to humans. Supplement 7: Overall evaluations of carcinogenicity: An updating of IARC monographs volumes 1 to 42, 186-189. IARC, Lyon.

2. International Agency for Research on Cancer (1991) Monographs on the evaluation of carcinogenic risks to humans. Volume 53: Occupational exposures in insecticide application, and some pesticides, 179-249. IARC, Lyon.

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Source: https://www.industrydocuments.ucsf.edu/docs/kmbl0000

42. Debrisoquine metabolism

Six studies were found which attempted to relate lung cancer risk to debrisoquine metabolism, and Table 42 gives details of them. Two estimates of relative risk were given, one of 0.61 for poor debrisoquine metabolizers and one of 6.1 for extensive metabolizers. One study reported that 78.8% of cases were extensive metabolizers compared to only 27.8% of controls, while another noted that 1.9% of cases were poor metabolizers compared to some 8.7% of the control group. Two studies failed to find any differences between cases and controls in the proportions of the metabolic types.

All of the studies were of a case-control design, and most assessed debrisoquine metabolism by administering the drug to respondents and classifying them phenotypically according to the rate of metabolism. However, it is possible that debrisoquine metabolism may be affected by the disease status of the subject [5], and in these studies it is not clear whether the observed differences in metabolic type were a cause or an effect of lung cancer. Only the study by Smith measured debrisoquine metabolism genotypically, thus avoiding this problem. In the light of this drawback, it is difficult to properly evaluate the possible association between lung cancer risk and debrisoquine metabolism suggested by the evidence presented in the table.

Table 42: Estimates of relative risk for debrisoquine metabolism

Study	Population	Relative risk (95% limits)
Ayesh et al (1984)	UK residents	78.8% of cases extensive metabolizers compared to 27.8% of controls
Roots et al (1988)	German residents	0.61(0.31-1.15)[1]
Law et al (1989)	UK residents	1.9% cases poor metabolizers compared to 8.7% of controls
Caporaso et al (1990)	US residents	6.1(2.2-17.1)[2]
Spiers et al (1990)	UK residents	No difference in proportion of poor metabolizers between cases and controls

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Table 42 continued

Smith et al (1992)	UK residents	No difference in proportion of poor metabolizers between cases and controls

1 Relative risk estimate for poor metabolizers
2 Relative risk estimate for extensive metabolizers

References

1. Ayesh R, Idle JR, Ritchie JC, Crothers MJ and Hetzel MR (1984) Metabolic oxidation phenotypes as markers for susceptibility to lung cancer. Nature, 312, 169-170.

2. Caporaso NE, Tucker MA, Hoover RN et al (1990) Lung cancer and the debrisoquine metabolic phenotype. JNCI, 82, 1264-1272.

3. Law MR, Hetzel MR and Idle JR (1989) Debrisoquine metabolism and genetic predisposition to lung cancer. Br J Cancer, 59, 686-687.

4. Roots I, Drakoulis N, Ploch M et al (1988) Debrisoquine hydroxylation phenotype, acetylation phenotype, and ABO blood groups as genetic host factors of lung cancer risk. Klin Wochenschr, 66, 87-97.

5. Smith CAD, Moss JE, Gough AC, Spurr NK and Wolf CR (1992) Molecular genetic analysis of the cytochrome P450-debrisoquine hydroxylase locus and association with cancer susceptibility. Environ Health Perspec, 98, 107-112.

6. Speirs CJ, Murray S, Davies DS, Biola Mabadeje AF and Boobis AR (1990) Debrisoquine oxidation phenotype and susceptibility to lung cancer. Br J Clin Pharmac, 29, 101-109.

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Source: https://www.industrydocuments.ucsf.edu/docs/kmbl0000

43. Dental mechanics

Details of the only study found which attempted to relate the risk of lung cancer to employment as a dental mechanic are given in Table 43. Three cases of lung cancer among men working as dental mechanics were reported, as was an increased risk of lung cancer found in two previous surveys, details of which were not available.

It was noted by the authors of the study that dental mechanics may be exposed to several potentially carcinogenic materials, including solvents, fumes, dust from abrasives and asbestos paper. It is therefore possible that any one of these may have caused the observed increase in lung cancer, but with no further information available it is not possible to determine which one, if any. Thus, the relationship between lung cancer risk and employment as a dental mechanic remains unclear.

Table 43: Observations for dental mechanics

Study	Population	Observations
Coggon et al (1986)	UK men	Three lung cancer cases worked as dental mechanics

References

1. Coggon D, Pannett B, Osmond C and Acheson ED (1986) A survey of cancer and occupation in young and middle aged men. I Cancers of the respiratory tract. Br J Ind Med, 43, 332-338.

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44. Dermatomyositis

Table 44 gives details of the only study found which attempted to investigate lung cancer risk in relation to dermatomyositis. It was reported that 14 cases of lung cancer were associated with dermatomyositis.

With so little information available it is not possible to evaluate the relationship between lung cancer and dermatomyositis, but it was thought unlikely that such an association existed [1].

Table 1: Observations for dermatomyositis

Study	Population	Observations
Williams (1959)	Hospital patients	14 cases of lung cancer associated with dermatomyositis

References

1. Roe FJC and Walters MA (1965) Some unsolved problems in lung cancer etiology. Progr Exp Tumor Res, 6, 126-227.

2. Williams RC (1959) Dermatomyositis and malignancy: A review of the literature. Ann Intern Med, 50, 1174-1181.

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Source: https://www.industrydocuments.ucsf.edu/docs/kmbl0000

45. 1,2-Dibromo-3-chloropropane

Only two studies could be found which gave any data relevant to an investigation of the possible association between lung cancer risk and exposure to 1,2-dibromo-3-chloropropane, and details of these are given in Table 45. One standardized mortality ratio, of 146, was calculated, while the other study stated that the increase in mortality observed was due mainly to an excess of respiratory cancers.

However, several drawbacks were noted with these studies. Workers in the study by Hearn had been exposed to arsenicals as well as 1,2-dibromo-3-chloropropane, but no information on the extent of exposure to either substance was given. Workers in the study by Wong were exposed to several brominated chemicals, but again no details of exposure were given.

In view of the numbers involved and the lack of control of confounding factors, IARC considered these studies to be "inadequate", as was the evidence for the carcinogenicity of 1,2-dibromo-3-chloropropane to humans [1].

Table 45: Estimates of standardized mortality ratio for exposure to 1,2-dibromo-3-chloropropane

Study	Population	Standardized mortality ratio
Hearn et al (1984)[1]	Chemical workers	Observed increase in mortality due mainly to excess of respiratory cancers
Wong et al (1984)[1]	US workers	146[2]

1 From International Agency for Research on Cancer (1987)

2 Estimated from data given

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Source: https://www.industrydocuments.ucsf.edu/docs/kmbl0000

References

1. International Agency for Research on Cancer (1987) Monographs on the evaluation of carcinogenic risks to humans. Supplement 7: Overall evaluations of carcinogenicity: an updating of IARC monographs volumes 1 to 42, 191-192. IARC, Lyon.

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46. Diesel engine exhausts

Table 46 lists the 30 studies found which gave details of a possible association between exposure to diesel engine exhausts and lung cancer. For cohort studies the estimates of relative risk ranged from 0.88-2.67, and standardized mortality ratios calculated were between 99 and 226, with 20 of the 26 reported results showing a positive association. The case-control studies showed a similar pattern, with relative risk estimates ranging from 0.60-2.70, with 21 out of 25 being above 1.00.

However, when considering these results, some important limitations in the design of the studies must be borne in mind. None of the studies included measurements of diesel exhaust concentrations during the actual exposure of the study population, relying instead on surrogate indices such as contemporary measurement of diesel soot in work environments similar to those used to classify past exposure, job history from interview, employment records or death certificates, and membership in a trade union. Additionally, further inaccuracies will be introduced due to the variable amount of time that subjects in different studies were required to have spent in a particular job or occupation in order to have been considered "exposed". Finally, many respondents exposed to diesel engine exhausts will have been exposed to other pollutants, particularly gasoline engine exhausts.

Not surprisingly then, a review by the US EPA [29] concluded that, due to methodological drawbacks, the evidence of carcinogenicity in humans was considered to be limited for diesel exhaust exposure. A more recent review [21] described the evidence of an association between exposure to diesel engine exhausts and lung cancer as "largely circumstantial", although it was felt that "taken in aggregate...the weight of the epidemiological evidence is convincing for a small positive effect." This is reflected by the categorization given by IARC, who describe diesel engine exhausts as "probably carcinogenic" (Group 2A) [17].

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Source: https://www.industrydocuments.ucsf.edu/docs/kmbl0000

Table 46: Estimates of relative risk/standardized mortality ratio for diesel engine exhausts

Study	Population	Relative risk (95% limits)
Cohort studies:		
Raffle (1957)	London transport employees	1.42
Kaplan (1959)	Baltimore/Ohio railroad workers	0.88
Waxweiler et al (1973)	US potash miners	No association
Leupker and Smith (1978)	US Teamsters Union Cohort	1.21(p > 0.05)
Ahlberg et al (1981)	Swedish male truck drivers	1.33(1.10-1.60)
Stern et al (1981)	New Jersey vehicle examiners	1.02
Waller (1981)	London transport employees	0.90(p > 0.05)
Howe et al (1983)	Canadian railroad workers	1.40(1.20-1.50)
Rushton et al (1983)	London bus maintenance workers	101 (82-122)*
Wong et al (1985)	US heavy equipment operators	99 (88-110)*
Gustafsson et al (1986)	Swedish dock workers	132 (105-166)*
Steenland (1986)	US teamsters - mechanics	226 (162-309)*
	truck drivers	154 (144-166)*
	dock workers	132 (99-175)*
	other	116 (95-142)*
Edling et al (1987)	Swedish bus company employees	<1.00
Boffetta et al (1988)	US males - miners	2.67(1.63-4.37)
	Heavy equipment operators	2.60(1.12-6.06)
	Railroad workers	1.59(0.94-2.69)
	Truck drivers	1.24(0.93-1.66)
Garshick et al (1988)	US railroad workers - age 40-44	1.45(1.11-1.89)
	age 45-49	1.33(1.03-1.73)
	age 50-54	1.20(p > 0.05)
	age 55-59	1.18(p > 0.05)
	age 60-64	0.99(p > 0.05)
Grandjean et al (1991)	Danish filling station attendants	1.58(1.25-2.00)

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Source: https://www.industrydocuments.ucsf.edu/docs/kmbl0000

Table 46 continued

Case-control studies:		
Menck and Henderson (1976)	LA County truck drivers	1.65($p < 0.05$)
Decoufle et al (1977)	US truck/bus/taxi drivers	0.92($p > 0.05$)
	US train engineers and firemen	0.94($p > 0.05$)
Williams et al (1977)	US male truck drivers	1.52($p > 0.05$)
Coggon et al (1984)	English/Welsh populations	1.30(1.10-1.60)
Hall and Wynder (1984)	US males	2.00(1.20-3.20)
	Heavy equipment repair/operators	1.90($p > 0.05$)
Buiatti et al (1985)	Italian male taxi drivers	1.80(1.00-3.40)
Damber and Larsson (1987)	Swedish professional drivers	1.20(0.90-2.60)
	Underground miners	2.70(1.20-6.00)
Garshick et al (1987)	US railroad workers	1.39(1.05-1.83)
Lerchen et al (1987)	New Mexicans exposed to diesel	0.60(0.20-1.60)
Benhamou et al (1988)	French motor vehicle drivers	1.42(1.07-1.89)
	Transport equipment operators	1.35(1.05-1.75)
	Miners and quarrymen	2.10(1.10-4.30)
Siemiatycki et al (1988)	Montreal males	1.20($p > 0.05$)
Hayes et al (1989)	US truck drivers > 10 years	1.50(1.10-1.90)
	All except truck drivers	1.30(1.00-1.70)
	Taxi drivers/chauffeurs <10 years	2.50(1.40-4.80)
	Taxi drivers/chauffeurs >10 years	1.20(0.50-2.60)
	Heavy equipment operators	2.10(0.60-7.10)
Boffetta et al (1990)	US males "probably exposed"	0.92(0.75-1.12)
	Self-reported exposure	1.26($p > 0.05$)
Steenland et al (1990)	US truck mechanics	1.69($p > 0.05$)
	Diesel truck drivers	1.42($p > 0.05$)

* Standardized mortality ratio

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47. Dietary fat/cholesterol and serum cholesterol

Table 47a gives details of the studies which considered dietary fat or cholesterol as a risk factor for lung cancer. It can be seen from this table that, of the 4 risk factors presented for low dietary intake, 2 are below 1.00 and 2 above, with the estimates of relative risk ranging from 0.60-2.70. For the studies which looked at high dietary intake the relative risk estimates ranged from 0.30-3.50, with 24 out of 32 being above 1.00, and only 8 risk estimates being 1.00 or below. Additionally, one study presented highly significant partial regression coefficients of 6.30 and 16.2, for age groups of 55-64 and 65-74 years respectively. However, as on the whole few confidence intervals were given, it is difficult to interpret the significance of these findings.

Table 47b lists the four prospective studies which attempted to measure serum cholesterol levels in relation to lung cancer risk. Two studies found some evidence of an increased risk in individuals with low serum cholesterol, although the results were only significant in one. However, the other two studies appeared to find a positive association between serum cholesterol level and lung cancer risk, with respondents in the lower cholesterol categories having a reduced risk.

However, several points should be considered when trying to interpret these results. Table 19a shows the wide variety of indices used to measure dietary fat intake, and it is not clear how accurately these may have measured fat intake. Additionally, most of the studies limited their subjects to men only, and so few results are available for women. Therefore, if any differences exist between the sexes they will be very difficult to spot.

Unlike nutrients such as vitamins A and C, it is well known that serum cholesterol is not highly correlated with dietary cholesterol, but rather with intake of saturated fat. Therefore, while the results from studies looking at dietary and at serum cholesterol may show few similarities, there should be some comparability in the findings of those studies measuring dietary fat intake and those measuring serum cholesterol. As discussed above, while most of the relative risks for high fat intake were above 1.00, the evidence for high serum cholesterol was less convincing.

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Finally, the onset of cancer may affect appetite and metabolism, so that patients may appear to have different levels of dietary and serum nutrients than non-sufferers. It has been suggested that the early stages of cancer cause a drop in serum cholesterol levels [7,8,10,14,15], so that subjects with lower levels may have a cancer that has not yet been detected. This is obviously a problem in case-control studies, and may also be so in prospective studies if the period of follow-up is not very long.

Table 47a: Estimates of relative risk for dietary cholesterol/fat intake

Study	Study type	Location	Index of fat intake	Relative risk (95% limits)
Low dietary intake:				
Mettlin et al (1979)	C-C	USA	Milk	1.60[1]
Wu et al (1985)	C-C	USA	Dairy products/ eggs	2.70[2]
Byers et al (1987)	C-C	USA	Total fat	0.60[3]
			Cholesterol	0.90[3]
High dietary intake:				
Hinds et al (1983)	C-C	USA	Cholesterol	1.75[3]
			Cholesterol	3.50(1.70-7.21)[1]
Kvale et al (1983)	PR	Norway	Milk	0.30[1]
			Meat	1.00[1]
			Eggs	0.90[1]
Heilbrun et al (1984)	PR	USA	Cholesterol	1.00[1]
Wynder et al (1987)	EC	43 countries	Total fat	>1.00(p <0.0001)[1]
				>1.00(p = 0.006)[2]
Goodman et al (1988)	C-C	USA	Total cholesterol	1.77(1.12-2.80)[3]
			Eggs	1.36(0.89-2.09)[3]
			Other sources	1.99(1.25-3.15)[3]
Mettlin (1989)	C-C	USA	Animal fat	1.50
			Whole milk	2.10
			Pork chops	2.40

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Table 47a continued

Jain et al (1990)	C-C	Canada	Cholesterol	1.55[3]
			Total fat	1.30
Fraser et al (1991)	PR	USA	Meat/fish/poultry	1.31(0.52-3.28)
			Milk	0.88(0.37-2.12)
Kesteloot et al (1991)	EC	34 countries	Dairy fat/lard	>1.00($p < 0.01$)[1]
				No association[2]
Knekt et al (1991)	PR	Finland	Cholesterol	1.03(0.58-1.85)[1]
			Total fat	1.55(0.78-3.10)[1]
			Saturated fat	1.64(0.84-3.19)[1]
			Monounsat. fat	1.07(0.56-2.05)[1]
			Polyunsat. fat	0.87(0.50-1.52)[1]
			P/S ratio	0.71(0.44-1.12)[1]
Shekelle et al (1991)	PR	USA	Cholesterol	1.94[1]
Xie et al (1991)	EC	29 countries	Animal fat	6.30(1.86-10.7)[5,6]
				16.2(9.19-23.2)[5,7]
Goodman et al (1992)	C-C	USA	Dairy products	2.19(1.40-3.43)[3]
			Processed meats	2.35(1.83-3.01)[3]
			Eggs	1.31(0.85-2.03)[3]
			Desserts	2.12(1.40-3.20)[3]
			Fried foods	1.42(0.89-2.29)[3]

C-C = Case-control; EC = Ecological; PR = Prospective; P/S = ratio of polyunsaturated to saturated fat

1 Males only

2 Females only

3 Estimated from data for males and females separately

4 Data from 43 countries

5 Partial regression coefficient

6 Age group 55-64 years only

7 Age group 65-74 years only

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Table 47b: Measurements of serum cholesterol levels in lung cancer patients and controls (Males only unless otherwise indicated)

Study	Location	Average cholesterol difference between cases and controls	Significance of difference
Kagan et al (1981)	USA	-20.30 mg/dl	$p < 0.01$
Law and Thompson (1991)	Various[1]	-0.181 mmol/l	$p > 0.05$[2]
		-0.041 mmol/l	$p > 0.05$[3]
		-0.106 mmol/l	$p > 0.05$[2,4]
		-0.032 mmol/l	$p > 0.05$[3,4]
		Cholesterol level	Relative risk (95% limits)
Knekt et al (1991)	Finland	215-248 mg/dl	0.80(0.40-1.50)
		249-285 mg/dl	1.10(0.60-1.80)
		>285 mg/dl	1.30(0.80-2.20)
Shekelle et al (1992)	USA	<5.53 mmol/l	0.90($p > 0.05$)
		5.53-6.13 mmol/l	0.70($p > 0.05$)
		6.14-6.90 mmol/l	1.00($p > 0.05$)
		≥6.91 mmol/l	1.00($p > 0.05$)

1 Combined results from 33 prospective studies

2 Short term studies (cancers presenting in first 5 years in mortality studies or first 2 years in incidence studies)

3 Long term studies (cancer presenting after 5 years in mortality studies or after 2 years in incidence studies)

4 Females only

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48. Dimethyl sulphate

No epidemiological studies concerning the risk of lung cancer in relation to exposure to dimethyl sulphate could be found, but two case reports of cancers following such exposure are shown in Table 48. A total of five cases of cancer of the lung and bronchus have been reported in workers occupationally exposed to dimethyl sulphate.

No objective measurements of the level of exposure of the cases were reported. In addition, it was stated that the case in the study by Bettendorf was also exposed to bis(chloromethyl)ether and chloromethyl methyl ether, both potent carcinogens, in higher concentrations than the exposure to dimethyl sulphate. It is clearly possible, then, that the observed pulmonary cancer could have been caused by exposure to substances other than dimethyl sulphate.

Although IARC stated that there was "some suspicion as to the possible carcinogenicity of dimethyl sulphate in man" [1], the evidence to support this was felt to be "inadequate" [2].

Table 48: Case reports following exposure to dimethyl sulphate

Study	Observation
Druckrey et al (1966)[1]	4 cases of bronchial carcinoma observed among chemical factory workers exposed to dimethyl sulphate.
Bettendorf (1977)[2]	1 case of pulmonary carcinoma after exposure to 'small amounts' of dimethyl sulphate.

1 From International Agency for Research on Cancer (1974)

2 From International Agency for Research on Cancer (1987)

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49. Dock workers

Only four studies were found which attempted to relate the risk of lung cancer to employment as a dock worker, and details of these are given in Table 49. Nine standardized mortality ratios were given, lying in the range 127-246, along with three proportional registration ratios, of between 122 and 143. Additionally, one proportional mortality ratio of 117 was presented, while another study estimated a relative risk of 1.46.

It was suggested that exposure to diesel exhaust may be an important factor in the development of lung cancer among dock workers [1]. However, only the study by Emmelin et al gave any information on the level of the workers' exposure, and this was not based on objective measurements but on an index of exposure, namely annual diesel fuel consumption. Therefore, it is difficult to assess lung cancer risk in terms of diesel exhaust exposure. Furthermore, it is likely that dock workers are exposed to other, potentially carcinogenic, substances such as asbestos [1], but as no measurements of workplace exposures were taken it is impossible to determine whether or not this is so.

The evidence presented in the table is consistent with an increased risk of lung cancer in dock workers. However, this information comes from a small number of studies and does not provide sufficient data to determine the nature of the subjects' exposures, nor the agent or agents responsible for the observed increase in risk.

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Table 49: Estimates of standardized mortality ratio/relative risk for dock workers

Study	Location	Subset	Standardized mortality ratio
OPCS (1978)	England	Men, 1970-72	117($p<0.05$)[1]
	and	1966-67	122($p<0.01$)[2]
	Wales	1968-69	125($p<0.01$)[2]
Logan (1982)	England	Men, 1931	183
	and	1951	149
	Wales	1961	169
		1971	182
		Married women[3], 1951	132
		1961	246
		1971	213
OPCS (1986)	Great	Men	136($p<0.01$)
	Britain	Married women[3]	127($p<0.01$)
		Men	143[2]
Emmelin et al (1993)	Sweden	Men	1.46(0.93-2.29)*

* Relative risk (95% limits)

1 Proportional mortality ratio

2 Proportional registration ratio

3 According to husband's occupation

References

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50. Epichlorohydrin

Only three studies were found which attempted to relate the risk of lung cancer to exposure to epichlorohydrin, and details of these are given in Table 50. Two standardized mortality ratios, of 80 and 137, were calculated, along with one relative risk of 2.4.

The main problem with these studies was the lack of information on the workers' exposures. Although the study by Barbone attempted to classify potential exposures this was based on interviews with the respondents and not on objective measurements. Additionally, no attempt was made to separate out the effects of epicholorohydrin and anthraquinone dye in those workers who had been exposed to both. Similar problems were noted in the study by Enterline, in which some workers had previously been exposed to isopropyl alcohol, and in the study by Tassignon, in which it was stated that workers had been exposed to a variety of chemicals but no data was available on which ones.

Therefore, with so few studies reporting, and noting the drawbacks mentioned above, it is difficult to reach any conclusions about the carcinogenicity of epicholorohydrin to humans. Not surprisingly then, IARC [2] classified the evidence as "inadequate".

Table 50: Estimates of standardized mortality ratio/relative risk for exposure to epichlorohydrin

Study	Population	Standardized mortality ratio
Enterline (1982)[1]	US factory workers	137*[2]
Tassignon et al (1983)[1]	European factory workers	80*[2]
Barbone et al (1992)	US dye/resin factory workers	2.4(1.1-5.2)*

* Relative risk

1 From International Agency for Research on Cancer (1987)

2 Estimated from data given

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References

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51. Family history of lung cancer/mendelian inheritance

Table 51 gives details of the studies which attempted to investigate lung cancer risk in relation to a family history of lung cancer. Fourteen relative risks were estimated, lying in the range 0.31-5.31, of which 12 were above 1.00. Two studies reported a 2.5- and a 3-fold excess of lung cancer among the relatives of cases, while another noted a family history of lung cancer among 9.3% of cases, compared to 4.8% of controls. One study found 21% of patients with primary lung cancer to have a family history of the disease, compared to only 6% of patients with secondary lung cancer and 6% of controls, and pairs of probands in which both members had lung cancer were found significantly more frequently than expected by one study. Case reports of lung cancer in close relatives were made by three studies, who noted the disease in four out of eight siblings over the age of 50, in two identical twins, and a total of 12 cases in two different families. Finally, one study reported findings compatible with a hypothesis of mendelian codominant inheritance of a rare autosomal gene producing an earlier age of onset of lung cancer in carriers.

It should be noted that bias arising from a variety of sources could have been introduced into the studies, and a more detailed discussion of this is given elsewhere [7]. Briefly, however, it was not thought that the results of the studies could be explained by confounding due to differences in age, smoking habits, family size or other variables, between the cases and controls, and recall bias was also not considered to be of great importance.

Therefore, there does appear to be evidence of an increased risk of lung cancer among subjects who have had a relative suffer from the same disease.

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Table 51: Estimates of relative risk for family history of lung cancer

Study	Location	Relative risk
Tokuhata and Lilienfeld (1963a)	US residents	2.5-fold excess of lung cancer among case relatives compared to controls
Tokuhata and Lilienfeld (1963b)	US residents	3-fold excess of lung cancer among case relatives compared to controls
Brisman et al (1967)	US residents	All four of eight siblings aged over 50 developed lung cancer
Joishy et al (1977)	US men	Identical twins developed lung cancers with similar time of onset, histochemistry and site of metastasis
Goffman et al (1982)	US residents	5 cases of lung cancer reported in one family and 7 cases reported in another
Alderson et al (1985)[1]	UK residents	1.28(0.93-1.78)
Ooi et al (1986)	US residents	3.07(1.1-8.7)
Samet et al (1986)	US residents	5.31(2.21-12.76)
Gao et al (1987)	Chinese women	1.1(0.6-2.3)[2] 3.0(0.7-12.5)[3]
Tsugane et al (1987)	Japanese men Women	1.67($p>0.05$) 0.31($p>0.05$)
Horwitz et al (1988)	US women	2.8(1.02-7.7)
McDuffie et al (1989)	Canadian residents	9.3% of cases had family history of lung cancer compared to 4.8% of controls ($p<0.005$)
Sellers et al (1990)	US residents	Results indicated compatibility of data with mendelian codominant inheritance of rare autosomal gene producing earlier age of onset of cancer
McDuffie (1991)	Canadian residents	1.99(1.18-3.37)

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Table 51 continued

Murata et al (1991)	Japanese women	Pairs of probands in which both members had lung cancer occurred significantly more frequently than expected
Osann (1991)	US women	1.9(0.7-5.6)
Shaw et al (1991)	US residents	2.8(1.2-6.6)
Sellers et al (1992)	US residents	1.9(0.9-4.1)[4]
Ambrosone et al (1993)	US residents, 0-20 years smoking	3.01(1.38-6.63)[5]
	21+ years	0.85(0.62-1.16)[5]
Pavlakou et al (1993)	Greek women	21% of primary lung cancer patients had family history of lung cancer compared to 6% of secondary lung cancer patients and 6% of controls

1 From Lee (1993)

2 Lung cancer in parents

3 Lung cancer in siblings

4 Small cell lung cancer compared to non-small cell lung cancer

5 Squamous cell/small cell cancers compared to large cell/adenocarcinomas

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52. Farmers/agricultural workers

Table 52 gives details of the studies which attempted to relate lung cancer risk to employment in the agricultural industry. Twenty-two standardized mortality ratios were calculated, ranging from 31-132, with 18 being below 100. In addition, five relative risks were estimated, ranging from 0.5-1.24, of which three were below 1.00. One proportional mortality ratio of 61 was also presented, along with a standardized mortality odds ratio of 929. These results are consistent with farmers and agricultural workers having a lower risk of lung cancer than workers in other industries.

One study put forward the theory that the lower incidence of lung cancer in farmers and farm workers is due to exposure to endotoxins which bring about a protective effect by stimulating macrophages to produce tumour necrosis factor, thus augmenting the body's defences against tumours. It was also suggested that exposure to tobacco smoke at low levels may have a similar effect, and that as farmers tend to smoke less than the general population this may be sufficient to explain their lower risk of lung cancer [8]. As little information was available from the studies on smoking habits it is not really possible to determine which of these explanations, if either, is the more likely.

In contrast, Benhamou et al suggested that the increased risk of lung cancer observed among farmers in their study could be explained by the use of arsenical insecticides [11]. Again, as none of the studies had collected information on such exposures, this hypothesis cannot be evaluated.

Overall, then, from the evidence presented in the table it can be seen that farmers and agricultural workers appear to have a decreased risk of lung cancer, but, as yet, no satisfactory explanations for this observation have been put forward.

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Table 52: Estimates of standardized mortality ratio/relative risk for farmers/agricultural workers

Study	Population	Standardized mortality ratio
OPCS (1978)	E/W male farmers/farm managers/ market gardeners	84[1]
	Agricultural workers	86
Logan (1982)	UK male farmers - 1931	35
	1951	46
	1961	59
	1971	57
	Married women - 1931	50
	1951	69
	1961	70
	1971	74
	UK male agricultural workers, 1931	31
	1951	51
	1961	77
	1971	105
	Married women[2] - 1931	29
	1951	74
	1961	88
	1971	118
Blot et al (1983)	US male agricultural workers	1.0(0.4-2.3)*
Milne et al (1983)	US male farmers	0.5($p<0.05$)*
	Farmers/farm labourers	0.8*
Dubrow and Wegman (1984)	US agricultural scientists	929($p<0.001$)[3]
OPCS (1986)	UK male farmers/horticulturists/ farm managers	47($p<0.01$)
	Married women[2]	57($p<0.01$)
	UK male farm workers	117($p<0.01$)
	Married women[2]	132
Benhamou et al (1988)	French farmers	1.24(0.94-1.62)*
Rylander (1990)	US male wheat/grain farmers	61($p<0.05$)[4]
Zappa et al (1993)	Italian agricultural workers	0.77(0.5-1.1)*

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Footnote to Table 52

E/W = English/Welsh

* Relative risk

1 Estimated from data given

2 According to husband's occupation

3 Standardized mortality odds ratio

4 Proportional mortality ratio

References

1. Benhamou S, Benhamou E and Flamant R (1988) Occupational risk factors of lung cancer in a French case-control study. Br J Ind Med, 45, 231-233.

2. Blot WJ, Brown LM, Pottern LM, Stone BJ and Fraumeni JF (1983) Lung cancer among long-term steel workers. Am J Epidemiol, 117, 706-16.

3. Dubrow R and Wegman DH (1984) Cancer and occupation in Massachusetts: A death certificate study. Am J Ind Med, 6, 207-230.

4. Logan WPD (1982) Cancer mortality by occupation and social class 1851-1971. HMSO, London and IARC, Lyon.

5. Milne KL, Sandler DP, Everson RB and Brown SM (1983) Lung cancer and occupation in Alameda County: A death certificate case-control study. Am J Ind Med, 4, 565-575.

6. Office of Population Censuses and Surveys (1978) Occupational mortality: The Registrar General's decennial supplement for England and Wales, 1970-72. HMSO, London.

7. Office of Population Censuses and Surveys (1986) Occupational mortality: The Registrar General's decennial supplement for Great Britain, 1979-80, 1982-83. HMSO, London.

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8. Rylander R (1990) Environmental exposures with decreased risks for lung cancer? Int J Epidemiol, 19 (Suppl 1), S67-S72.

9. Zappa M, Paci E, Seniori Costantini A and Kriebel D (1993) Lung cancer among textile workers in the Prato area of Italy. Scand J Work Environ Health, 19, 16-20.

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53. Fishermen

The five studies found which investigated a possible association between lung cancer risk and employment as a fisherman are detailed in Table 53. Three relative risks were estimated, ranging from 1.0-3.2, with two being above 1.00. Two proportional mortality ratios, of 125 and 144, were also given, along with one standardized mortality ratio of 205.

It can be seen, then, that there is a fairly consistent increase in the risk of lung cancer among fishermen, but as yet no plausible mechanism for this observation has been put forward. One study suggested that the excess of lung cancers was probably more a reflection of the way way of life of fishermen, particularly their drinking and smoking habits, than a direct consequence of the occupation [2]. However, elsewhere it was felt that the persistence of the raised PMR after the removal of other causes of death individually large enough to seriously affect it added support to the hypothesis that fishermen are at excess risk of lung cancer [3]. Unfortunately, there is not really sufficient data for a full evaluation to be made.

Table 53: Estimates of relative risk/standardized mortality ratio for fishermen

Study	Location	Subset	Relative risk(95% limits)
OPCS (1978)	England/Wales		205*[1]
Gottlieb et al (1979)[2]	US		1.8
Blot et al (1982)[2]	US		3.2
Howe and Lindsay (1983)[3]	Canada		1.00
OPCS (1986)	UK	Aged 15-64	144[4]
		Aged 65-74	125[4]

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Footnote to Table 53

* Standardized mortality ratio

1 Estimated from data given

2 From Williams Pickle (1984)

3 From Blot (1984)

4 Proportional mortality ratio

References

1. Blot WJ (1984) Lung cancer and occupational exposures. In: Lung cancer: Causes and prevention, 47-64. Verlag Chemie International Inc.

2. Office of Population Censuses and Surveys (1978) Occupational mortality: The Registrar General's decennial supplement for England and Wales, 1970-72. HMSO, London.

3. Office of Population Censuses and Surveys (1986) Occupational mortality: The Registrar General's decennial supplement for Great Britain, 1979-80, 1982-83. HMSO, London.

4. Williams Pickle L, Correa P and Fontham E (1984) Recent case-control studies of lung cancer in the United States. In: Lung cancer: Causes and prevention, 101-115. Verlag Chemie International Inc.

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Source: https://www.industrydocuments.ucsf.edu/docs/kmbl0000

54. Fishmongers/poultry dressers

Table 54 gives details of the only study which attempted to investigate the possible association between lung cancer risk and working as a fishmonger or poultry dresser. A standardized mortality ratio of 273 was calculated. Separate findings for the two occupations were not presented.

It was suggested that, as with butchers, the excess of lung cancers observed may have arisen from the handling of raw flesh, but with only one study reporting it is not possible to properly evaluate this hypothesis, or determine if there is a relationship between lung cancer risk and employment as a fishmonger or poultry dresser.

Table 54: Estimate of standardized mortality ratio for fishmongers/ poultry dressers

Study	Population	Standardized mortality ratio
OPCS (1986)	UK men	273

References

1. Office of Population Censuses and Surveys (1986) Occupational mortality: The Registrar General's decennial supplement for Great Britain, 1979-80, 1982-83. HMSO, London.

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Source: https://www.industrydocuments.ucsf.edu/docs/kmbl0000

55. Formaldehyde

Table 55 presents details of the studies which gave data relevant to an investigation of the possible association between lung cancer risk and exposure to formaldehyde. The seven relative risks which were estimated ranged from 0.34-1.11, with only one being above 1.00. Two standardized mortality ratios, of 97 and 136, were also presented, along with one proportional mortality ratio of 102.

From the table it can be seen that subjects drawn from the medical professions show a consistent decrease in lung cancer risk, an observation which has been noted elsewhere, and it has been suggested that this deficit might be explained by the lower prevalence of tobacco use in these occupational groups [2]. However, insufficient data on the subjects' smoking habits was given by the studies to determine whether or not this was the case. Little information was also given about the level of exposure of the subjects, with only the study by Partanen giving broad categories of exposure, while only the study by Wong had attempted to identify other substances the subjects may have been exposed to. These include oxygenated hydrocarbons other than formaldehyde, benzene, asbestos, and inorganic and organic pigments. Embalming fluid also contains a variety of chemicals apart from formaldehyde [1]. Thus, it is possible that workers were exposed to other substances which were themselves potentially carcinogenic, and this may have introduced bias into the results.

While those working in the medical professions appear to show a decreased risk of lung cancer in relation to formaldehyde exposure, studies of workers manufacturing or using formaldehyde have given less conclusive results. This led IARC to classify the evidence for the carcinogenicity of formaldehyde to humans as "limited" [2].

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Table 55: Estimates of relative risk/standardized mortality ratio for exposure to formaldehyde

Study	Population	Relative risk (95% limits)
Doll and Peto (1976)[1]	British doctors	1.00
Doll and Peto (1977)[1]	UK male scientific researchers/ pathologists/biochemists	<1.00
OPCS (1978)	E/W qualified medical practitioners	<1.00
Jensen and Andersen (1982)	Danish doctors ever employed in pathology, forensic medicine or anatomy	1.0(0.4-2.4)
Walrath and Fraumeni (1982)[1]	US embalmers	102[2,3]
Wong (1982)[1]	US male chemical factory workers	97*[3,4]
Bertazzi et al (1986)[5]	Italian formaldehyde-resin plant workers	136*
Partanen (1993)	Anatomists, pathologists, forensic medicine specialists	0.34(0.26-0.44)[6]
	Funeral directors, embalmers, undertakers, drug users	0.98(0.89-1.07)[6]
	Industrial workers	1.11(1.03-1.19)[6]

* Standardized mortality ratio

1 From International Agency for Research on Cancer (1982)

2 Proportional mortality ratio

3 Tumours of respiratory system

4 Estimated from data given

5 From International Agency for Research on Cancer (1987)

6 Combined results from 9 studies

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Source: https://www.industrydocuments.ucsf.edu/docs/kmbl0000

References

1. International Agency for Research on Cancer (1982) Monographs on the evaluation of the carcinogenic risk of chemicals to humans. Volume 29: Some industrial chemicals and dyestuffs, 345-389. IARC, Lyon.

2. International Agency for Research on Cancer (1987) Monographs on the evaluation of the carcinogenic risks to humans. Supplement 7: Overall evaluations of carcinogenicity: An updating of IARC monographs volumes 1 to 42, 211-216. IARC, Lyon.

3. Jensen OM and Andersen SK (1982) Lung cancer risk from formaldehyde. The Lancet, Apr 17, 913. (Letter)

4. Office of Population Censuses and Surveys (1978) Occupational mortality: The Registrar General's decennial supplement for England and Wales, 1970-72. HMSO, London.

5. Partanen T (1993) Formaldehyde exposure and respiratory cancer - a meta-analysis of the epidemiological evidence. Scand J Work Environ Health, 19, 8-15.

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56. Fruits and vegetables

Lack of time meant that a full evaluation of the possible association between lung cancer risk and fruit and/or vegetable consumption could not be presented in this document. However, the studies dealing with this area have been included, where relevant, in the sections for vitamins A and C. All presented evidence suggestive of a protective effect of fruit and/or vegetable intake on lung cancer risk.

As with other dietary variables, it is possible that the development of cancer may affect appetite and thus lead to changes in fruit and/or vegetable consumption which are a result of the disease rather than a cause of it. Thus, findings from prospective studies may be more reliable than those from case-control studies. It is also possible that a high intake of fruit and/or vegetables may be correlated with some other dietary variable which is itself protective for lung cancer, or there may be an inverse correlation with a dietary factor, such as fat, which is thought to be positively associated with lung cancer risk.

Overall, the evidence for a protective effect of fruit and/or vegetable intake is more consistent than that for any one particular nutrient, although the mechanism responsible for this effect remains unclear.

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57. Fuel oils

Only five studies were found which gave data relevant to an investigation of the possible association between lung cancer risk and exposure to fuel oils and details of these are given in Table 57. Five relative risks, ranging from 1.4-2.7, were calculated. One study reported that while 91% of the case group had used kerosene stoves, only 36% of the controls had done so.

None of the studies appeared to have taken objective measurements of the exposures the respondents were subjected to, although the studies by Koo and Siematycki did attempt to classify exposure levels. Furthermore, subjects in the study by Tsuchiya were exposed to several substances, including kerosene, diesel oil, crude petroleum and mineral oil, while those in the studies by Chan, Leung and Koo were more likely to have been exposed to the combustion products of kerosene rather than to kerosene itself. Exposure to cooking oil may also have contributed to the observed effects in these studies. Finally, problems in the statistical analysis of the study by Tsuchiya were noted [1].

Thus, IARC stated that while residual (heavy) fuel oils were "possibly carcinogenic to humans", distillate (light) fuel oils were "not classifiable as to their carcinogenicity". Overall, it was felt that there was "inadequate" evidence for the carcinogenicity of fuel oils to humans [1].

Table 57: Estimates of relative risk for exposure to fuel oils

Study	Population	Relative risk (95% limits)
Tsuchiya (1965)[1]	Japanese workers	2.7(1.4-5.3)
Siematycki et al (1987)[1]	Canadian men	1.7(1.2-3.4)
Leung (1977)[1]	Hong Kong women	Kerosene stoves used by 91% cases and 36% controls
Chan et al (1979)[1]	Hong Kong women	1.6(0.99-2.6)
Koo et al (1983)[1]	Hong Kong women, smokers	2.5(1.2-5.4)
	Non-smokers	1.4(1.1-1.9)

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Source: https://www.industrydocuments.ucsf.edu/docs/kmbl0000

Footnote to Table 57

1 From International Agency for Research on Cancer (1989)

References

1. International Agency for Research on Cancer (1989) Monographs on the evaluation of carcinogenic risks to humans. Volume 45: Occupational exposures in petroleum refining; crude oil and major petroleum fuels, 239-270. IARC, Lyon.

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58. Gasoline engine exhaust

The five studies which gave data relevant to an investigation of the possible association between lung cancer risk and exposure to gasoline engine exhaust are detailed in Table 58. Six relative risks were estimated, and they ranged between 1.2 and 1.8.

A number of potential problems were identified in the studies. Firstly, since exposure to engine exhaust is nearly ubiquitous in urban areas 'unexposed' reference groups are likely to contain a large number of individuals who are in fact exposed non-occupationally. Secondly, the studies assessed the subjects' exposure indirectly, as no measurements of exposure level appeared to have been taken. In fact, all of the studies except the one by Siemiatycki relied on job title as a surrogate for exposure to gasoline engine exhaust. This may obviously have introduced inaccuracies into these studies. Lastly, some of the study subjects may have been exposed to other potentially carcinogenic substances, particularly diesel engine exhausts, and again this may have affected the results.

Therefore, IARC considered that gasoline engine exhaust could only be described as "possibly carcinogenic to humans [2].

Table 58: Estimates of relative risk for exposure to gasoline engine exhaust

Study	Population	Relative risk (95% limits)
Buiatti et al (1985)[1]	Italian taxi drivers	1.8(1.0-3.4)
Damber and Larsson (1987)[1]	Swedish professional drivers, dead controls	1.5(0.9-2.6)
	Live controls	1.7(0.9-3.2)
Benhamou et al (1988)[1]	French motor vehicle drivers	1.4(1.1-1.9)
Siemiatycki et al (1988)[1]	Canadian men aged 35-70 years	1.2(1.0-1.4)[2]
Grandjean and Andersen (1991)	Danish filling station attendants	1.58(1.25-2.0)

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Source: https://www.industrydocuments.ucsf.edu/docs/kmbl0000

Footnote to Table 58

1 From International Agency for Research on Cancer (1989)

2 90% confidence interval

References

1. Grandjean P and Andersen O (1991) Lung cancer in filling station attendants. Am J Ind Med, 20, 763-768.

2. International Agency for Research on Cancer (1989) Monographs on the evaluation of carcinogenic risks to humans. Volume 46: Diesel and gasoline engine exhausts and some nitroarenes, 41-185. IARC, Lyon.

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59. General labourers

Four studies were found which investigated the possible association between lung cancer risk and employment as a general labourer and details of these are given in Table 59. Ten standardized mortality ratios, lying in the range 84-270, were calculated, of which eight were raised. In addition, two proportional mortality ratios, of 106 and 109, were presented, along with two proportional registration ratios, of 115 and 119, and one relative risk estimate of 0.9.

None of the studies gave any information on the possible exposures of the subjects, and no hypotheses were put forward to explain the increase in lung cancer risk observed. Thus, although the evidence presented in the table appears to suggest a slightly higher risk of lung cancer among general labourers, it is not possible to identify any potentially carcinogenic agents which may have been responsible for this increase.

Table 59: Estimates of standardized mortality ratio/relative risk for general labourers

Study	Population	Standardized mortality ratio
OPCS (1978)	E/W male labourers/unskilled workers aged 15-64	109($p<0.01$)[1]
	Aged 65-74	106($p<0.01$)[1]
	Incidence 1966-7	115($p<0.01$)[2]
	1968-9	119($p<0.01$)[2]
Logan (1982)	E/W male labourers - 1931	96
	1951	169
	1961	161
	1971	199
	Married women[3] - 1931	84
	1951	106
	1961	147
	1971	193

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Table 59 continued

Milne et al (1983)	US male general labourers	0.9*
OPCS (1986)	British male labourers	246(p<0.01)
	Married women[3]	270(p<0.01)

E/W = English/Welsh

* Relative risk

1 Proportional mortality ratio

2 Proportional registration ratio

3 According to husband's occupation

References

1. Logan WPD (1982) Cancer mortality by occupation and social class 1851-1971. HMSO, London.

2. Milne KL, Sandler DP, Everson RB and Brown SM (1983) Lung cancer and occupation in Alameda County: A death certificate case-control study. Am J Ind Med, 4, 565-575.

3. Office of Population Censuses and Surveys (1978) Occupational mortality: The Registrar General's decennial supplement for England and Wales, 1970-72. HMSO, London.

4. Office of Population Censuses and Surveys (1986) Occupational mortality: The Registrar General's decennial supplement for Great Britain, 1979-80, 1982-83. HMSO, London.

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60. Glass workers

Only three studies were found which contained data relevant to an investigation of the possible association between lung cancer risk and working in the glass manufacturing industry and details of these are given in Table 60. Two relative risks, of 2.0 and 2.2, were estimated, and one standardized incidence ratio of 128 was also presented.

Glass workers may be exposed to various potentially carcinogenic substances, including arsenic, metals and asbestos [1,3]. However, none of the studies made any attempt to measure the workers' exposures and thus it is difficult to identify the agent or agents responsible for producing the observed increase in lung cancer risk among glass workers. In any case, from the evidence presented in the table it can be seen that any increase in risk, if it does exist, is not likely to be particularly large.

Table 60: Estimates of relative risk/standardized incidence ratio for glass workers

Study	Population	Relative risk (95% limits)
Milne et al (1983)	US glass manufacturing workers	2.2($p<0.05$)
Wingren and Axelson (1985)[1]	Swedish glass blowers	2.00
Sankila et al (1990)	Finnish glass factory workers	128(99-162)

* Standardized incidence ratio

1 From International Agency for Research on Cancer (1987)

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References

1. International Agency for Research on Cancer (1987) Monographs on the evaluation of carcinogenic risks to humans. Supplement 7: Overall evaluations of carcinogenicity: An updating of IARC monographs volumes 1 to 42, 100-106. IARC, Lyon.

2. Milne KL, Sandler DP, Everson RB and Brown SM (1983) Lung cancer and occupation in Alameda County: A death certificate case-control study. Am J Ind Med, 4, 565-575.

3. Sankila R, Karjalainen S, Pukkala E et al (1990) Cancer risk among glass factory workers: An excess of lung cancer? Br J Ind Med, 47, 815-818.

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61. Gold mining

Details of the five studies found which presented data relevant to the investigation of a possible association between lung cancer and gold mining are given in Table 61. Four relative risks were estimated, ranging from 1.4-7.9, along with one standardized mortality ratio of 100. Finally, one study calculated an annual incidence rate of 205.6/100 000, compared to the general male population.

Gold miners are thought to have potential exposure to several substances which may be carcinogenic, and those which have been discussed include arsenic, asbestos, chromium, nickel, radon and silica [1-5]. However, only two of the studies [1,2] attempted to make any objective measurements of workers' exposures and, with the exception of asbestos [2], all of the above-named substances were found only in very low concentrations, below levels which are thought to pose any risk. Thus, the possible role of any individual exposure is very hard to ascertain.

Although the data presented in the table is consistent with an increase in lung cancer risk among gold miners, the lack of information on exposures such workers are subjected to makes it very difficult to identify the agent or agents responsible. One study which found high levels of asbestos but negligible levels of arsenic, chromium, nickel and radon felt that this was sufficient evidence for the excess of respiratory disease observed to be attributed to asbestos exposure [2]. However, no data was available from the other studies to back this up.

Table 61: Estimates of relative risk/standardized mortality ratio for gold miners

Study	Population	Relative risk (95% limits)
Osburn (1957)[1]	Rhodesian gold miners	205.6[2]
Gillam et al (1976)	South Dakota gold miners	2.70($p<0.05$)[3]
Armstrong et al (1979)	Australian gold miners	1.4($p<0.01$)[3]
Katsnelson and Mokronosova (1979)[4]	Russian gold miners - underground	7.9($p<0.001$)
	Surface	1.6
Brown et al (1986)[5]	US gold miners	100*

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Source: https://www.industrydocuments.ucsf.edu/docs/kmbl0000

Footnote to Table 61

* Standardized mortality ratio

1 From International Agency for Research on Cancer (1980)

2 Incidence rate per 100 000 per year

3 Tumours of respiratory system

4 From Goldsmith et al (1982)

5 From International Agency for Research on Cancer (1987)

References

1. Armstrong BK, McNulty JC, Levitt LJ, Williams KA and Hobbs MST (1979) Mortality in gold and coal miners in Western Australia with special reference to lung cancer. Br J Ind Med, 36, 199-205.

2. Gillam JD, Dement JM, Lemen RA et al (1979) Mortality patterns among hard rock gold miners exposed to an asbestiform mineral. Ann N Y Acad Sci, 271, 336-344.

3. Goldsmith DF, Guidotti TL and Johnston DR (1982) Does occupational exposure to silica cause lung cancer? Am J Ind Med, 3, 423-440.

4. International Agency for Research on Cancer (1980) Monographs on the evaluation of the carcinogenic risk of chemicals to humans. Volume 23: Some metals and metallic compounds, 39-142. IARC, Lyon.

5. International Agency for Research on Cancer (1987) Monographs on the evaluation of the carcinogenic risk of chemicals to humans. Volume 42: Silica and some silicates, 39-144. IARC, Lyon.

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62. Haematite and iron oxide

Table 62 gives details of the studies which attempted to relate the risk of lung cancer to exposure to haematite and iron oxide. Ten studies calculated standardized mortality ratios, ranging from 100-176, of which half were raised, while another study reported a raised standardized incidence ratio but did not give details of the results. One study observed a lung cancer incidence 10.7 times higher among iron ore miners than among non-miners, while another reported bronchial cancer to be 2.29 times higher in such workers. Three other studies observed lung cancer incidence of 9.4% in haematite miners compared to 2.0% in controls, bronchogenic carcinoma incidence of 3.3% in iron ore miners compared to 1.5% in controls, and a lung cancer mortality rate of 6.6 per 10,000 compared to the national rate of 4 per 10,000. A further three studies reported that lung cancer mortality was higher in the population of interest than in the controls, but did not give any further details. A total of seven lung or bronchial cancers were observed in the remaining three studies.

No information was available from the studies on the level of exposure to haematite and iron oxide, as none appeared to have attempted to quantify exposure in any way. Thus, it is obviously possible that inaccuracies could have been introduced into the results. Furthermore, the study subjects came from a range of occupations, some of which entail exposure to other substances which may themselves be potentially carcinogenic. For example, miners may be exposed to silica and radon, while welding involves exposure to many metals, particularly zinc. Boiler scalers may be exposed to both silica and soot. In the absence of exposure data it is not possible to determine which, if any, of these substances subjects may have come into contact with, or the potential carcinogenicity of any one material.

Therefore, IARC appear to be justified in their classification of the evidence for the carcinogenicity of haematite and iron oxide to humans as "inadequate". However, the evidence for underground haematite mining with exposure to radon was considered "sufficient" [4].

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Source: https://www.industrydocuments.ucsf.edu/docs/kmbl0000

Table 62: Estimates of standardized mortality ratio for exposure to haematite and iron oxide

Study	Population	Standardized mortality ratio
Stewart and Faulds (1934)[1]	Haematite miners	1 bronchial cancer observed
Vorwald and Karr (1937,1938)[1]	Haematite miners	3 lung cancers observed
Turner and Grace (1938)[1]	UK foundry workers/ metal grinders	Lung cancer mortality higher than in other occupations
McLaughlin et al (1945)[1]	Silver finishers	100
Barrie and Harding (1947)[1]	Silver finishers	100
Kennaway and Kennaway (1947)[1]	UK metal grinders	176
Harding (1948)[1]	Silver finishers	100
McLaughlin et al (1950)[1]/ McLaughlin and Harding (1956)[1]	UK iron/steel foundry workers	>100[2]
Harding and Massie (1951)[1]	Boiler scalers	3 lung cancers observed
Wynder and Graham (1951)[1]	Welders/hot metal workers	Lung cancer cases more often hot metal workers than other diseases
Doll (1953)[1]	Welders/hot metal workers	100
Breslow et al (1954)[1]	Welders/hot metal workers	Lung cancer cases more often hot metal workers than other diseases
Faulds and Stewart (1956)	UK haematite miners	Lung cancer incidence 9.4% vs. 2.0% controls
Podhrazsky (1957)[1]	Czech steel plant workers	Mortality rate 6.6[3] vs. 4 nationally
Braun et al (1960)[1]	French iron-ore miners	Bronchogenic carcinoma incidence 3.3% vs. 1.5% in controls (p=0.01)

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Table 62 continued

Monlibert and Roubille (1960)[1]	French iron-ore miners	Bronchial cancer incidence 2.29 times higher than in controls
Gurevich (1967)[1]	USSR iron-ore miners	Lung cancer mortality 10.7 times higher than among non-miners
Boyd et al (1970)	UK haematite miners	168[4]
Anthoine et al (1979)[5]	French iron ore miners	>100
Axelson and Sjoberg (1979)[5]	Iron foundry workers	100
Tola et al (1979)[5]	Iron foundry workers	>100
Lawler et al (1985)[5]	US iron ore miners	100

1 From International Agency for Research on Cancer (1972)

2 Standardized incidence ratio

3 Per 10,000

4 Estimated from data given

5 From International Agency for Research on Cancer (1987)

References

1. Boyd JT, Doll R, Faulds JS and Leiper J (1970) Cancer of the lung in iron ore (haematite) miners. Br J Ind Med, 27, 97-105.

2. Faulds JS and Stewart MJ (1956) Carcinoma of the lung in haematite miners. J Path Bacteriol, 72, 353-366.

3. International Agency for Research on Cancer (1972) Monographs on the evaluation of carcinogenic risk of chemicals to man. Volume 1, 29-39. IARC, Lyon.

4. International Agency for Research on Cancer (1987) Monographs on the evaluation of carcinogenic risks to humans. Supplement 7: Overall evaluations of carcinogenicity: An updating of IARC monographs volumes 1 to 42, 216-219. IARC, Lyon.

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63. Hairiness of 2nd phalanx

Table 63 gives details of the only study found which attempted to relate lung cancer risk to hairiness of the 2nd phalanx. It was reported that 3.1% of cancer cases had a hairy 2nd phalanx compared to only 2.1% of controls.

The authors themselves stated that multiple comparisons result in some apparent association due to chance alone, and that the observed relationship between lung cancer risk and hairiness of the 2nd phalanx may be a case in point.

Table 63: Observations on hairiness of 2nd phalanx

Study	Population	Observations
Denoix et al (1958)	French men	3.1% bronchial cancer cases had hairy 2nd phalanx compared to 2.1% controls

* Standardized mortality ratio

References

1. Denoix PF, Schwartz D and Anguera G (1958) French investigation into the etiology of broncho-pulmonary cancer. Detailed analysis. Bull Assoc Franc pour l'etude du cancer, 49: 1-37.

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Source: https://www.industrydocuments.ucsf.edu/docs/kmbl0000

64. Hashimoto's thyroiditis

Table 64 gives details of the only study found which presented data relevant to an investigation of the possible association between lung cancer risk and Hashimoto's thyroiditis. A standardized mortality ratio of 209 was calculated.

With so little information available it is not possible to evaluate the relationship between lung cancer and Hashimoto's thyroiditis.

Table 64: Estimate of standardized mortality ratio for Hashimoto's thyroiditis

Study	Population	Standardized mortality ratio
Yamashita et al (1979)	Japanese women	209($p<0.05$)[1]

1 Estimated from data given

References

1. Yamashita N, Maruchi N and Mori W (1979) Hashimoto's thyroiditis: A possible risk factor for lung cancer among Japanese women. Cancer Letters, 7, 9-13.

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Source: https://www.industrydocuments.ucsf.edu/docs/kmbl0000

65. Hexachlorocyclohexanes

Table 65 gives details of the only study found which investigated the possible association between lung cancer risk and exposure to hexachlorocyclohexanes (HCH). A standardized mortality ratio of 180 was calculated.

However, it should be noted that the workers in this study received their exposure through the application of various pesticides, and thus exposure could be to compounds other than HCH, or in addition to HCH. Therefore, IARC felt that it was not possible to evaluate the carcinogenicity of HCH to humans on the basis of this study [1] and classified the evidence as "inadequate" [2].

Table 65: Estimate of standardized mortality ratio for exposure to hexachlorocyclohexanes

Study	Population	Standardized mortality ratio (95% limits)
Barthel (1976)[1]	Agricultural workers	180(140-240)

1 From International Agency for Research on Cancer (1987)

References

1. International Agency for Research on Cancer (1979) Monographs on the evaluation of carcinogenic risk of chemicals to humans. Volume 20: Some halogenated hydrocarbons, 195-223. IARC, Lyon.

2. International Agency for Research on Cancer (1987) Monographs on the evaluation of carcinogenic risks to humans. Supplement 7: Overall evaluations of carcinogenicity: an updating of IARC monographs volumes 1 to 42, 220-222. IARC, Lyon.

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66. History of lung disease

Details of the studies which investigated the possible association between lung cancer risk and a history of previous lung disease are given in Table 66. Relative risks ranging between 0.76-29.82 were estimated, with 55 out of 62 being above 1.00. Two standardized proportionate mortality ratios, both of 1.50, were also estimated. In addition, one study reported a positive association but did not give any detailed results, while two others stated that tuberculosis patients and pneumonia patients were 20 and 100 times more likely to develop lung cancer than the general population respectively, and one study reported that 10.0% of male and 8.2% of female lung cancer cases had a history of tuberculosis infection. Finally, one study reported finding a correlation between lung cancer mortality in adulthood and tuberculosis mortality in the period corresponding to the childhood of the lung cancer cases.

Most of the studies gathered information on history of lung disease from registers or medical records, or followed-up groups of patients with lung diseases, but several (Alavanja, Campbell, Campbell and Hughes, Wu, Wynder, Wynder and Fairchild) appeared to have based their data on information elicited at interviews with the subjects or their next-of-kin. It is obvious that this could have led to inaccuracies due to mistakes in recalling disease status, particularly in those studies which collected health data from a surrogate respondent. Additionally, no details were given at all on how the data on tuberculosis infection were collected in the study by Zheng.

Although results for several diseases were presented in the table, apart from tuberculosis, and to a lesser extent pneumonia, very few studies reported on each disease. Thus, with the exception of tuberculosis, an unequivocal relationship was not seen for any of the diseases considered. The data presented in the table suggest a positive association between lung cancer risk and a history of tuberculosis infection, but on the whole the estimates of relative risk are not particularly large, and therefore the relationship does not appear to be very strong. Furthermore, a recent review of lung cancer and tuberculosis stated that although patients with active pulmonary tuberculosis had a higher than normal risk of dying from lung cancer, there was "little biological evidence of TB lesions themselves, or TB bacilli per se,

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having major roles to play in the carcinogenesis of lung cancer at the moment" [2].

Table 66: Estimates of relative risk for history of lung disease

Study	Population	Dis-ease	Relative risk (95% limits)
Wynder et al (1956)[1]	Women	PNEU	1.00
		TB	1.00
Campbell and Hughes (1960)[1]	Not stated	TB	Lung cancer occurred 20 times more frequently in TB patients than general population
Campbell (1961)[1]	Not stated	TB	Positive association
Steinitz (1965)[2]	Israeli residents	TB	10.0% male and 8.2% female lung cancer cases had history of TB
Wynder and Fairchild (1966)	US men	ANY	4.28(2.79-6.56)[3]
		ASTH	3.93(1.18-13.1)[3]
		EMPH	0.93(0.09-9.24)[3]
		INJ	0.76(0.20-2.88)[3]
		PLEU	2.49(1.29-4.80)[3]
		PNEU	1.70(0.99-2.93)[3]
		TB	0.84(0.22-3.21)[3]
Simecek and Simeckova (1967)[2]	Czech residents	TB	4.2
Aoki et al (1969)[2]	US white men	TB	6.7(4.0-9.6)
	Non-white men	TB	8.6(4.0-13.7)
	US white men active	TB	10.5
	Non-white men "	TB	20.6
	White men, inactive	TB	4.5
	Non-white men "	TB	2.3
	US residents, 1962-3	TB	3.6(1.9-5.3)
	1963-4	TB	1.7(0.4-3.0)
	Japanese men	TB	2.75
	Women	TB	5.48

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Table 66 continued

Aoki et al (1969)[2]/ Ipsen (1967)[2]	US men	TB	3.1
Campbell and Guilfoyle (1970)[2]	Australian men	TB	2.06
Kreus et al (1970)[2]	Finnish residents	TB	2.2
Aoki and Ohtani (1971)[2]	Japanese men, 1964-68	TB	1.41[4]
			1.23[5]
	Women	TB	1.33[4]
			1.54[5]
	Men, 1974-82	TB	4.21[4]
			2.13[6]
	Women,	TB	3.87[4]
			2.16[6]
Watanabe and Kurashima (1977)[2]	Japanese residents	TB	3.56
	Japanese residents	TB	6.93
Clemmensen and Hjalgrim-Nelson (1979)[2]	Danish men, INH+	TB	3.36
	INH-	TB	2.58
	Women, INH+	TB	4.55
Howe et al (1979)[2]	Canadian men	TB	1.50(1.21-1.47)[7]
	Women	TB	1.50(1.11-1.98)[7]
Hongo et al (1981)[2]	Japanese men	TB	4.88
	Women	TB	9.69
Komatsu et al (1981)[2]	Japanese men	TB	2.58
	Women	TB	19.6
Mercer (1981)	English residents	TB	Correlation between lung cancer mortality in adulthood and TB mortality in time period corresponding to childhood
Hinds et al (1982)	Hawaiian women	TB	1.0(0.2-5.5)
	Japanese women	TB	2.0(0.4-10.3)
	Chinese women	TB	2.1(0.3-16.1)
Aoki (1985)[2]	Japanese men	TB	12.0
	Women	TB	5.0

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Table 66 continued

Takatorige et al (1985)[2]	Japanese residents, -1 year follow-up	TB	29.82
	1-2 years	TB	6.36
	2-3 years	TB	5.00
	3-4 years	TB	4.35
	4-5 years	TB	1.27
	5+ years	TB	1.27
Zheng et al (1987)[2]	Chinese residents	TB	1.5(1.2-1.8)
Wu et al (1988)	Not stated	TB	10.0(1.1-90.1)
Sakurai et al (1989)[2]	Japanese women	TB	6.4
Gao et al (1991)[2]	Chinese men	TB	1.72(1.11-2.53)
	Women	TB	2.79(1.79-4.14)
Alavanja et al (1992)	US female residents	ANY	1.2(1.0-1.5)
		ASTH	1.3(0.8-2.1)
		EMPH	2.6(1.5-4.7)
		PLEU	0.9(0.7-1.3)
		PNEU	1.2(1.0-1.6)
		TB	2.0(1.0-4.1)
Ohtsuka et al (19??)	Japanese men	PNEU	Pneumonia sufferers 100 times more likely to develop lung cancer than general population

ANY = any previous lung disease; ASTH = asthma; EMPH = emphysema; INH = Isoniazid treatment; INJ = lung injury; PLEU = pleurisy; PNEU = pneumonia; TB = tuberculosis

1 From Roe and Walters (1965)

2 From Aoki (1993)

3 Estimated from data given

4 Cardiovascular disease controls

5 Gastric cancer controls

6 Ischaemic heart disease controls

7 Standardized proportionate mortality ratio

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Source: https://www.industrydocuments.ucsf.edu/docs/kmbl0000

References

1. Alavanja MCR, Brownson RC, Boice JD and Hock E (1992) Preexisting lung disease and lung cancer among nonsmoking women. Am J Epidemiol, 136, 623-632.

2. Aoki K (1993) Excess incidence of lung cancer among pulmonary tuberculosis patients. Jpn J Clin Oncol, 23, 205-220.

3. Hinds MW, Cohen HI and Kolonel LN (1982) Tuberculosis and lung cancer risk in nonsmoking women. Am Rev Resp Dis, 125, 776-778.

4. Mercer AJ (1981) Risk of dying from tuberculosis or cancer: Further aspects of a possible association. Int J Epidemiol, 10, 377-380.

5. Ohtsuka Y, Tanimura K, Munakata M et al (19??) Idiopathic interstitial pneumonia(IIP) as a risk factor for a lung cancer - a prospective study. Incomplete reference.

6. Roe FJC and Walters MA (1965) Some unsolved problems in lung cancer etiology. Progr Exp Tumor Res, 6, 126-227.

7. Wu AH, Yu MC, Thomas DC, Pike MC and Henderson BE (1988) Cancer Res, 48, 7279-7284.

8. Wynder EL and Fairchild EP (1966) The role of a history of persistent cough in the epidemiology of lung cancer. Am Rev Resp Dis, 94, 709-720.

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67. Hormone therapy in women

Details of the only study found which presented data relevant to an investigation of lung cancer risk in women in relation to having received hormone therapy are given in Table 67. A relative risk of 1.26 was estimated.

With only one study reporting it is not possible to properly evaluate the relationship between lung cancer risk and hormone therapy in women.

Table 67: Estimate of relative risk for hormone therapy in women

Study	Population	Relative risk (95% limits)
Adami et al (1989)	Swedish women	1.26(0.92-1.68)

References

1. Adami H-O, Persson I, Hoover R, Schairer C and Bergkvist L (1989) Risk of cancer in women receiving hormone replacement therapy. Int J Cancer, 44, 833-839.

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68. Hydrazine and derivatives

The five studies found which attempted to relate the risk of lung cancer to exposure to hydrazine and its derivatives are detailed in Table 68. One study looked at exposure to hydrazine itself, while the other four considered isonicotinic acid hydrazide (INH). Seven relative risks were estimated overall, of between 1.10 and 4.6.

None of the studies gave any information on the level of exposure to hydrazine or INH, simply stating whether or not exposure had taken place. In fact, in the study by Hammond, it was stated that only 10% of one of the groups of patients had been exposed to INH. Thus, a raised relative risk was observed among a group of patients who were predominately not exposed to INH.

Not surprisingly, IARC felt there was "inadequate" evidence for the carcinogenicity to humans of both hydrazine and INH [2].

Table 68: Estimates of relative risk for exposure to hydrazine and its derivatives

Study	Population	Exposure	Relative risk (95% limits)
Hammond et al (1967)[1]	TB patients	INH	1.23(p>0.05)[2]
	TB patients	INH	1.59(p>0.05)[2]
Campbell and Guilfoyle (1970)[1]	Male TB patients	INH	1.10(p>0.05)[2]
Stott et al (1976)[3]	TB patients	INH	1.6(1.2-2.1)
Clemmensen and Hjalgrim-Jensen (1979)[3]	Male TB patients	INH	3.4
	Female TB patients	INH	4.6
Wald et al (1984)[3]	Male factory workers	HYD	1.2(0.2-4.5)

HYD = hydrazine; INH = isonicotinic acid hydrazide

1 From International Agency for Research on Cancer (1974)

2 Estimated from data given

3 From International Agency for Research on Cancer (1987)

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Source: https://www.industrydocuments.ucsf.edu/docs/kmbl0000

References

1. International Agency for Research on Cancer (1976) Monographs on the evaluation of carcinogenic risk of chemicals to man. Volume 4: Some aromatic amines, hydrazine and related substances, N-nitroso compounds and miscellaneous alkylating agents, 159-172. IARC, Lyon.

2. International Agency for Research on Cancer (1987) Monographs on the evaluation of carcinogenic risks to humans. Supplement 7: Overall evaluations of carcinogenicity: An updating of IARC monographs volumes 1 to 42, 223-224 and 227-228. IARC, Lyon.

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69. Hypercalcaemia

Table 69 gives details of the only two studies found which attempted to relate the risk of lung cancer to the presence of hypercalcaemia. A total of 6 lung cancers were observed in association with hypercalcaemia.

With so few studies reporting, and in the absence of any estimates of risk, it is not possible to properly evaluate the relationship between lung cancer and hypercalcaemia.

Table 69: Observations for hypercalcaemia

Study	Population	Observations
Connor et al (1956)	US men	2 cases reported in which hypercalcaemia disappeared after removal of lung tumour
Tashjian (1963)	US residents	4 cases of lung cancer associated with hypercalcaemia

References

1. Connor TB, Thomas WC and Howard JE (1956) The etiology of hypercalcemia associated with lung carcinoma. Am Soc Clin Invest, 35, 697-698.

2. Tashjian AH (1963) Case records of the Massachusetts General Hospital. N Engl J Med, 269, 801-813.

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70. Hypertrophic pulmonary osteoarthropathy

Only two studies were found which gave information relevant to an investigation of the possible association between lung cancer risk and hypertrophic pulmonary osteoarthropathy (HOA), and details of these are presented in Table 70. One study reported that 3-4% of lung cancer cases were also suffering from HOA, while the other noted that 13 of the 14 cases of lung cancer associated with HOA arose from peripherally located tumours, rather than centrally located ones.

Various explanations of the association between the two conditions were put forward, but with so few studies reporting it is not possible to evaluate the relationship between lung cancer and HOA.

Table 70: Observations for hypertrophic pulmonary osteoarthropathy

Study	Population	Observations
Ray and Fisher (1953)	US residents	13 out of 14 cases of HOA associated with lung cancer arose from peripherally located tumours
Coury (1960)	French residents	3-4% lung cancer cases also have HOA

References

1. Coury C (1960) Hippocratic fingers and hypertrophic osteoarthropathy: A study of 350 cases. Br J Dis Chest, 54, 202-209.

2. Ray ES and Fisher HP (1953) Hypertrophic osteoarthropathy in pulmonary malignancies. Ann Intern Med, 38, 239-246.

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71. Iron/steel founding

Table 71 details the numerous studies found which gave some data on the risk of lung cancer in those employed in iron and steel founding and allied occupations. Standardized mortality ratios (SMR) in the range 129-233 were presented by those studies which concentrated on mortality statistics. Three studies gave proportional mortality ratios (PMR), of 123, 170 and 186. The cohort studies showed a similar pattern, with the 25 SMRs presented lying in the range 0-714, with all but one being raised. Two PMRs, of 144 and 147, were also given. Additionally, seven studies produced estimates of relative risk of between 0.96 and 1.39, five of which were above 1.00. Finally, three case-control studies presented eight relative risks of between 1.20 and 7.10. Detailed results were not available from the fourth case-control study, which simply stated that cases were more often floor moulders, coremakers, casters and fettlers than controls.

Iron and steel workers may be exposed to a variety of potentially hazardous substances, including airborne crystalline silica from quartz sand used in moulding and coremaking, metallic fumes present during melting, pouring, welding and flame-cutting, metal dusts associated with abrasive grinding operations, carbon monoxide emitted from the cupola and casting operations, phenol, formaldehyde, furfuryl alcohol, isocyanates and amines used as ingredients of organic binders in mould and core sands, and pyrolysis products, such as polynuclear aromatic compounds, formed as a result of the contact between molten metal and carbonaceous materials during pouring [2]. No information was available from any of the studies as to the actual exposures of the workers, and therefore it is not possible to separate out the effects of any one substance, or even to say which substances the subjects were exposed to.

Despite this drawback, the consistent excess of lung cancer deaths seen in iron and steel foundry workers suggests that certain occupational exposures may be risk factors, and this is reflected in the ratings given by IARC, which stated that such exposures were "probably" carcinogenic [2], although it was later felt that the evidence for carcinogenicity to humans was "sufficient" [3].

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Source: https://www.industrydocuments.ucsf.edu/docs/kmbl0000